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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/972,301	11/18/97	COLEMAN T	325800-588(P

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EXAMINER
KEMMERER,E

ART UNIT	PAPER NUMBER
1646	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/972,301	Applicant(s) Coleman et al.
	Examiner Elizabeth C. Kemmerer	Group Art Unit 1646

☒ Responsive to communication(s) filed on *12 Nov 1998*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *39-42, 45-47, and 57-78* is/are pending in the application.

Of the above, claim(s) *39-42 and 45-47* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *57-78* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *39-42, 45-47, and 57-78* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The amendment filed 12 November 1998 (Paper No. 6) has been entered in full. Claims 1-38, 43, 44, and 48-56 are canceled. Claims 39-42 and 45-47 are pending and withdrawn from consideration as being directed to a non-elected invention. Claims 57-78 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection of claims 22 and 29 under 35 U.S.C. § 112, first paragraph, as set forth at pp. 5-6 of the previous Office Action (Paper No. 3, 14 May 1998) is *withdrawn* in view of the canceled claims.

The rejection of claims 21 and 32 under 35 U.S.C. § 112, first paragraph, as set forth at pp. 7-8 of the previous Office Action (Paper No. 3, 14 May 1998) is *withdrawn* in view of the canceled claims.

The rejection of claims 21, 22, 29, 32, and 36 under 35 U.S.C. § 112, second paragraph, as set forth at pp. 8-9 of the previous Office Action (Paper No. 3, 14 May 1998) is *withdrawn* in view of the canceled claims.

The objection to claims 23-28, 30, 31, 33-35, 37, and 38 as set forth at p. 9 of the previous Office Action (Paper No. 3, 14 May 1998) is *withdrawn* in view of the canceled claims.

The previous Examiner's indication of allowable subject matter is also withdrawn. Consequently, the instant office action is made non-final.

35 U.S.C. § 112, First Paragraph

Claims 57, 59, 60, 62, 64, 65, 67, 68 and 70-76 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. The claims recite ATCC Deposit No. 97132. This ATCC number is never mentioned in the specification. It appears that the claims submitted in Paper No. 2 (18 November 1998), now canceled, and Paper No. 6 (12 November 1998), pending, contain a typographical error wherein ATCC Deposit No. 97165 was intended. However, Applicant is strongly encouraged to carefully review their records regarding this matter, and to note that it appears that related application 08/483,584 has been allowed with claims reciting ATCC Deposit No. 97165.

Claims 65-70, 72, 73, 75 and 76 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 65-70, 72, 73, 75 and 76 embrace biologically active variants of the polypeptide disclosed as comprising the amino acid sequence set forth as residues 1-168 of SEQ ID NO: 2 or the polypeptide encode by the deposited human cDNA (for the purposes of this rejection, it will be assumed that Applicant intended the claims to recite ATCC Deposit No. 97165). The variants differ from either of these two defined compounds by one or more conservative amino acid substitutions or by being encoded by a polynucleotide which hybridizes to the compliment of SEQ ID NO: 1 or the deposited human cDNA. For the claims reciting "hybridizing" language, no stringency conditions are specified, and thus even polypeptides encoded by polynucleotides which hybridize under conditions of very low stringency, wherein the polypeptides have a biological activity of the polypeptide of 1-168 of SEQ ID NO: 2, are embraced. Since most polypeptides have a biological activity of being a nutritional supplement, or of inducing an immunological response when injected into a heterologous host, these claims embrace virtually any polypeptide. The specification discloses polypeptides comprising the amino acid sequence of 1-168 of SEQ ID NO: 2 or the sequence encoded by the deposited human cDNA clone

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the polypeptides comprising the amino acid sequence of 1-168 of SEQ ID NO: 2 or the sequence encoded by the deposited human cDNA clone, the skilled artisan cannot envision the detailed chemical structure of the encompassed variant polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only polypeptides comprising the amino acid sequence of 1-168 of SEQ ID NO: 2 or the sequence encoded by the deposited human cDNA clone, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 57-77 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to polypeptides comprising amino acid residues 1-168 of SEQ ID NO: 2, the amino aid sequence encoded by the deposited human cDNA clone (for the purposes of this rejection, it will again be assumed that Applicant intended the claims to recite ATCC Deposit No. 97165), fragments and variants thereof which share a biological activity of the polypeptide consisting of 1-168 of SEQ ID NO: 2, and fragments thereof at least 30 contiguous amino acids in length. Dependent claims 71-76 are directed to fusion proteins comprising these polypeptides and compositions comprising these polypeptides plus a pharmaceutically acceptable carrier. The specification discloses EMAP III which has the structure of 1-168 of SEQ ID NO: 2 or is encoded by the deposited human cDNA clone. EMAP III shares significant sequence identity with a polypeptide known as EMAP II. Based on this sequence identity, the specification speculates that EMAP III has similar biological activities to EMAP II. No biological activities have been specifically demonstrated for EMAP III. The assertion that EMAP III has similar biological activities as EMAP II cannot be accepted in the absence of supporting evidence, because the relevant literature reports examples of closely related polypeptides belonging to a polypeptide family wherein individual members have distinct, and sometimes even opposite, biological activities. For example, Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF-β family members

BMP-2 and TGF-β1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Similarly, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone 14:717-720; see p. 717, second paragraph of Introduction). Thus, the specification fails to teach the skilled artisan how to use EMAP III and variants thereof without resorting to undue experimentation to determine what the specific biological activities of EMAP III are.

The specification does not teach the skilled artisan how to use the disclosed EMAP III for purposes unrelated to the asserted biological activity. For example, there is no evidence of tissue-specific expression patterns, such that the EMAP III protein could be used as a tissue-specific marker. Similarly, there is no disclosure of particular disease states correlating to an alteration in levels or forms of EMAP III such that EMAP III could be used as a diagnostic tool. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polypeptides or any purpose.

Due to the large quantity of experimentation necessary to determine an activity or property of EMAP III such that it can be determined how to use EMAP III, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot b predicted based on structural similarity, and the breadth of the claims which fail to recite particular biological activities and also embrace a broad class of structural fragments and variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 112, Second Paragraph

Claims 65-67, 72, and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Independent claim 65 recites "said amino acid sequence" at lines 3-4 and 5, 8, and 9. There is no clear antecedent basis for this phrase in the claim, since the term "amino acid sequence" appears in the preamble of the claim and in the first phrase of each of parts (a) and (b). Furthermore, it is not clear how a polypeptide can comprise a fully defined amino acid sequence (e.g., 1-168 of SEQ ID NO: 2) *and* conservative amino acid residues substitution. Dependent claims 66, 67, 72, and 75 are included in this rejection since they depend from claim 65 and do not correct the deficiency. The following is suggested for claim 65 in order to overcome the issue under 35 U.S.C. § 112, second paragraph: "An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: (a) a variant of the amino acid sequence shown as residues 1 to 168 of SEQ ID NO: 2, wherein said variant differs from the amino acid sequence shown as residues 1 to 168 of SEQ ID NO: 2 by one or more conservative amino acid residue substitutions, ... (b) a variant of the amino acid sequence of the mature polypeptide encoded by the human cDNA contained in ATCC Deposit No. 97132, wherein said variant differs from the amino acid sequence of the mature polypeptide encoded by the human cDNA contained in ATCC Deposit No. 97132 by one or more conservative amino acid residue substitutions....."

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 68-70, 73 and 76 are rejected under 35 U.S.C. 102(e) as being anticipated by Stern et al., U.S. Patent 5,641,867.

Stern et al. teach EMAP II, a polypeptide comprising an amino acid sequence encoded by a polynucleotide which would hybridize to the complement of the nucleotide sequence set forth as SEQ ID NO: 1 or the human cDNA in ATCC Deposit No. 97165 (again, for the purposes of this rejection, it is assumed that the claims were intended to recite ATCC Deposit No. 97165 instead of 97132). See Figures 4A-4D. The polypeptide has a biological activity of a polypeptide consisting of 1-168 of SEQ ID NO: 2, in that it can be used as a nutritional supplement, or in that it induces an immunological response when injected into a heterologous host (column 6, lines 27-33). Stern et al. also teach the polypeptide fused to a heterologous polypeptide (column 6, lines 18-30), and a composition comprising the polypeptide and a pharmaceutically acceptable carrier (column 8, lines 44-50).

Sequence Rules

The instant application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, because each disclosure of a sequence embraced by the definitions set forth in the rules is no accompanied by the required reference to the relevant sequence identifier (i.e., SEQ ID NO:). This occurs at least at p. 32.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D., whose telephone number is (703) 308-2673. The examiner can normally be reached on Mondays through Thursdays from 6:30 a.m. to 4:00 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703) 308-2731.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

ECK
January 31, 1999